

Figure 1. Polymer aqueous/aqueous emulsion system.

Polymer solution A and polymer solution B are immiscible, thus A can be dispersed into B under a shear stress. The third polymer carries charge and is fairly immiscible with both A and B at low concentration, so that it tends to be rich at the interface of A and B, and forms a charged surface. The charged surface effectively prevent aggregation and fusion of the dispersed phase (See *Example 1* in the paragraph). Therapeutic agents such as proteins, liposomes and viruses are partitioned and encapsulated in the dispersed phase and subjected to lyophilization (See *Examples 2, 3 and 4*).

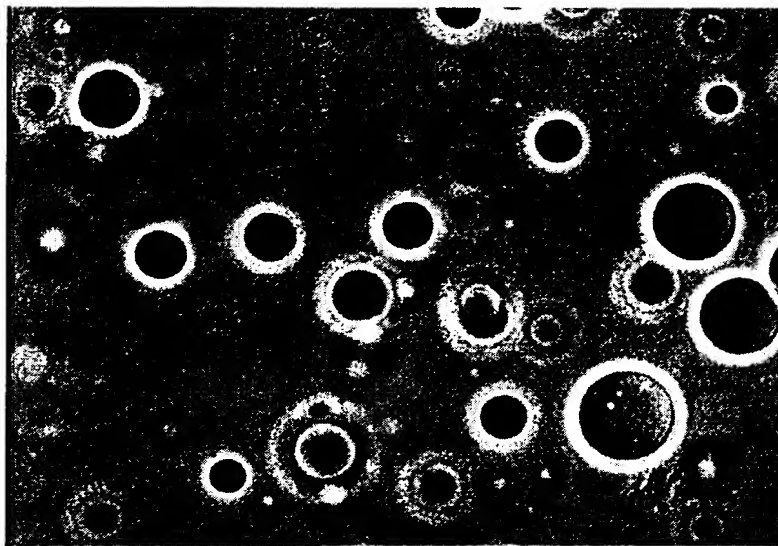


Figure 2. Microscopic image of polymer aqueous/aqueous emulsion

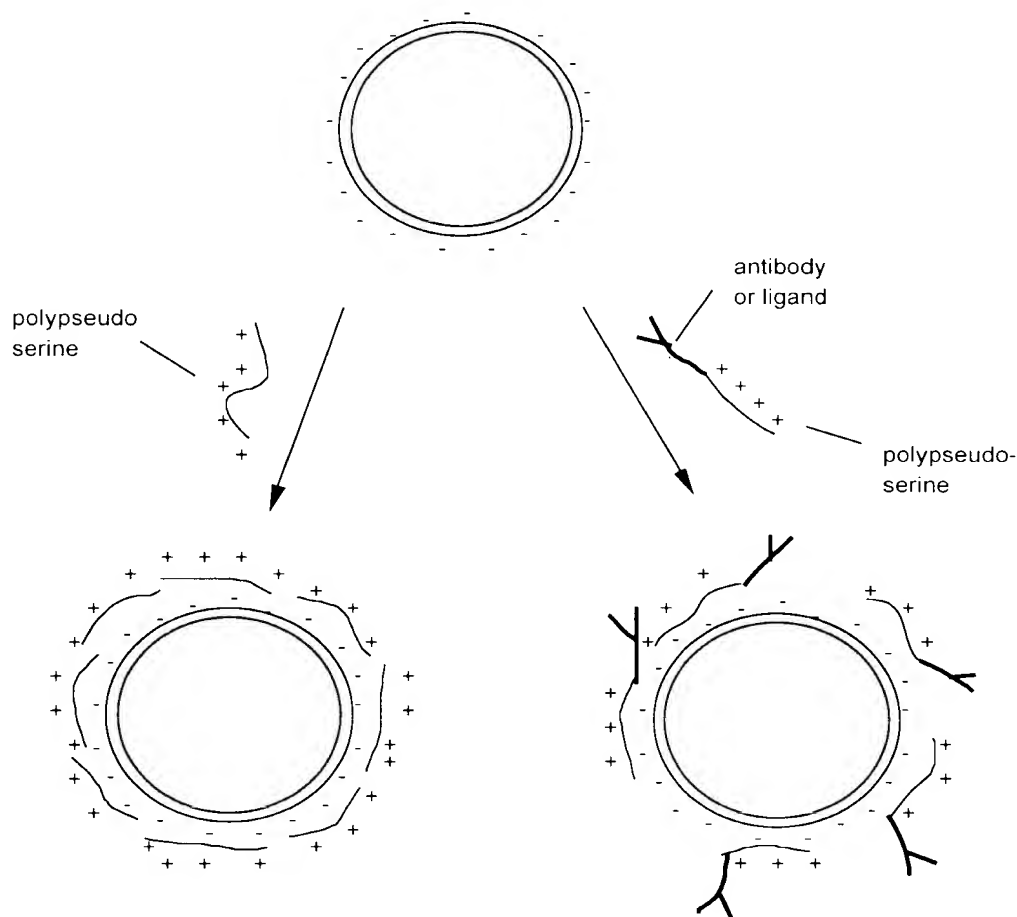
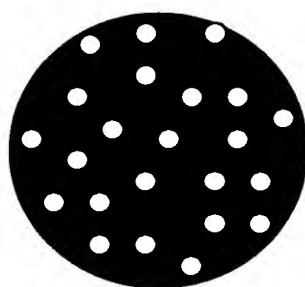


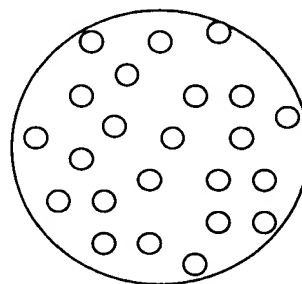
Figure 3. Secondary surface modification of polymer aqueous droplets dispersed in a polymer aqueous continuous phase.

The surface of the dispersed phase in Figure 1 can be further modified for functionization (See *Additional applications* in the paragraph). Permeability barrier can be assembled on the surface by ionic cross-linking with a degradable polymer having opposite charge, or by assembly of a lipid bilayer having opposite charge. Release rate of encapsulated therapeutics can be adjusted by selecting the cross-linking polymer in terms of chain length and structure of desired degradation rate (polyaminoacid or polypeptide for example). Targeting moieties (antibodies or ligands) can be immobilized on the surface through ionic interaction or hydrophobic interaction (in the case of lipid bilayer assembly).



A

Pre-washed before second microencapsulation. The matrix is more hydrophobic.



B

Un-washed before second microencapsulation. The matrix is less hydrophobic.

Figure 4. Microspheres prepared by double-microencapsulation through solid-in-oil-in-water emulsification

The powder formed by drying of the aqueous/aqueous emulsion can be further encapsulated into hydrophobic, degradable polymer microspheres. Since methane dichloride, a commonly used solvent in polymer microsphere preparation, dissolves reactant B (the continuous phase of the A/A emulsion) but does not interact with reactant A (the dispersed phase), reactant B can be removed from the lyophilized powder simply by washing with the solvent. Microspheres which encapsulate the lyophilized powder possess more hydrophobic matrix if reactant B is washed out, but less hydrophobic if reactant B remains. This structural difference can affect degradation rate of the polymer matrix and diffusion rate through the polymer matrix, thus the release profile of offers encapsulated therapeutics can be adjusted by the content of reactant B remained.

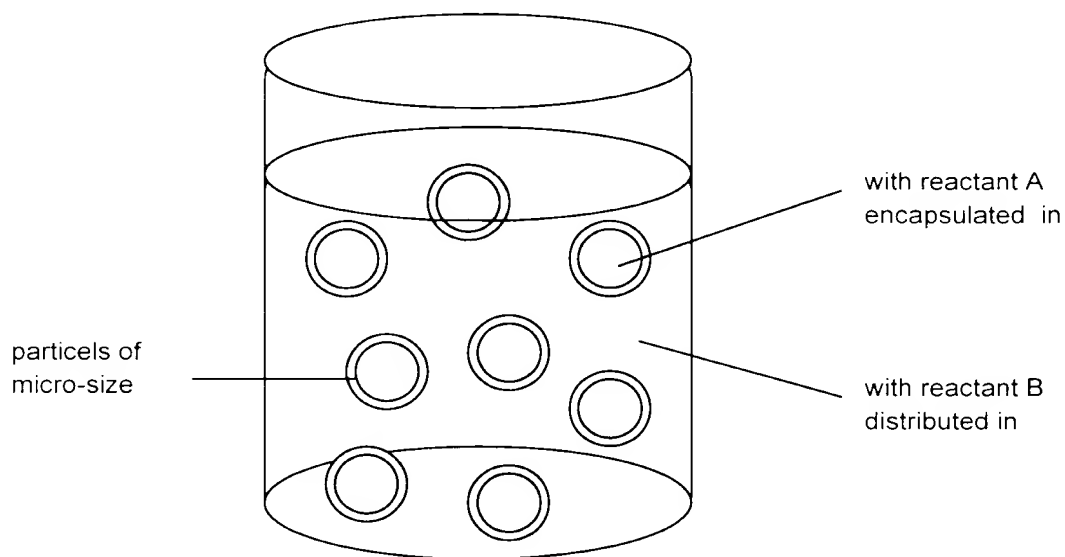


Figure 5. Nano-sized preparation using polymer aqueous/aqueous emulsion.

Nano-meter-sized crystals and other assemblies formed from two reactants can be prepared using the emulsion system (See reference [14]). Reactant A is usually those which partitioned and encapsulated into the dispersed phase. Reactant B is those which are distributed to both phases. Since A is isolated with limited quantity in each micro-sized droplet, when the assembly process proceeds, the limited accessibility of the reactants ensures a small sized product. Nano-sized preparation is useful in produce of both therapeutic and diagnostic agents.



Figure 6. Microscopic image of reconstituted AmB/liposomes (of SUV) which were freeze-dried after loading into the polymer emulsion. (The bright particle is a reference for focusing.)

Liposomes are not visible due to size, indicating that the small unilamellar structure is protected by the polymer emulsion system.

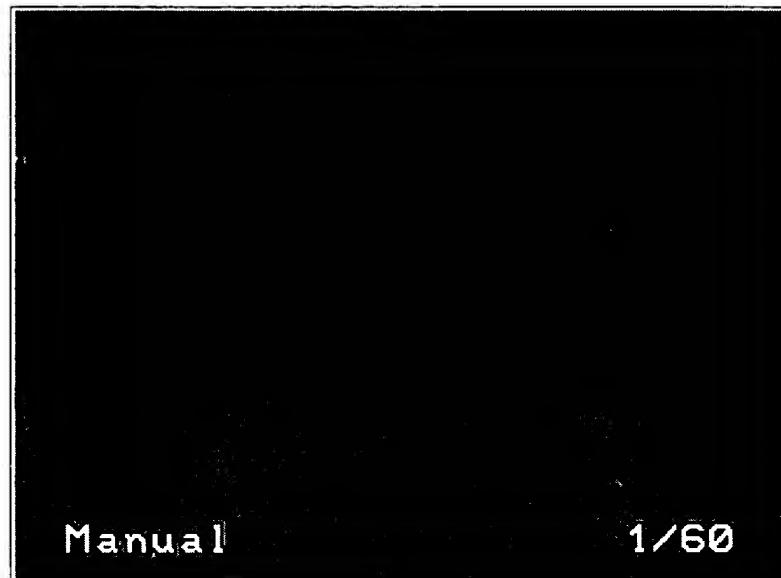


Figure 7. Microscopic image of reconstituted AmB/SUV which were freeze-dried without loading into the polymer emulsion.

Liposome particles are observed after reconstitution (re-hydration) of the small unilamellar liposomes after lyophilization without protection by the polymer emulsion system.